More people with depression continued treatment with fluoxetine than with desipramine or imipramine


QUESTION: In patients with depression, does initial treatment with fluoxetine improve clinical, quality of life, and economic outcomes better than treatment with desipramine or imipramine?

Design
Randomised (allocation concealed*), unblinded*, controlled trial with 24 months of follow up.

Setting
Primary care clinics in a health maintenance organisation in Seattle, Washington, USA.

Patients
536 patients (median age 41 y, 72% women) who were beginning antidepressant drug treatment. Exclusion criteria were use of antidepressant drugs in the previous 90 days, alcohol abuse, psychotic symptoms, history of mania, recent lithium or antipsychotic medication, or contraindication to the study drug. Follow up was 81% at 12 months and 72% at 24 months.

Intervention
Patients were stratified by presence or absence of current major depression and allocated to fluoxetine (n = 173), desipramine (n = 181), or imipramine (n = 182).*

Main outcome measures
Continuing use of initial medication; remission of depression; change in Hamilton Depression Rating Scale (HDRS) scores and Hopkins Symptom Checklist (HSCL) depression subscale score; change in SF-36 Mental Component Summary (MCS) score; and cost.

Main results
Patients who began antidepressant treatment with fluoxetine were more likely to continue taking it but not more likely to continue taking any antidepressant medication. Clinical and quality of life outcomes improved within 6 months of treatment and did not differ between fluoxetine, desipramine, and imipramine.

Conclusions
Patients who began antidepressant treatment with fluoxetine were more likely to continue taking it but not more likely to continue taking any antidepressant medication. Clinical and quality of life outcomes improved within 6 months of treatment and did not differ between fluoxetine, desipramine, and imipramine.

*See glossary.

Patients continuing initial antidepressant medication: fluoxetine (Flu) v desipramine (Des) and imipramine (Imi)*

<table>
<thead>
<tr>
<th>Follow up</th>
<th>Comparison</th>
<th>Event rates</th>
<th>RBI (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>Flu v Des</td>
<td>58% v 30%</td>
<td>92% (47 to 153)</td>
<td>4 (3 to 6)</td>
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<tr>
<td></td>
<td>Flu v Imi</td>
<td>58% v 36%</td>
<td>60% (25 to 105)</td>
<td>5 (4 to 10)</td>
</tr>
<tr>
<td>12 months</td>
<td>Flu v Des</td>
<td>42% v 20%</td>
<td>107% (43 to 201)</td>
<td>5 (4 to 10)</td>
</tr>
<tr>
<td></td>
<td>Flu v Imi</td>
<td>42% v 27%</td>
<td>56% (13 to 117)</td>
<td>7 (4 to 25)</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RBI, NNT, and CI calculated from data supplied by author.

COMMENTARY
This “real life” study by Simon et al gives us insight into how antidepressants are used in practice and the associated costs. Randomised controlled trials with economic modelling tell us a limited amount about the real world. We know that newer drugs cost more but we don’t know how their putative benefits translate into outcome or cost effectiveness.

In this study, the lower rate of switching because of adverse effects suggests that fluoxetine was better tolerated than tricyclics; outcome and willingness to continue taking antidepressants, however, was not affected. The human cost of this difference is difficult to know. Starting treatment with fluoxetine led to greater drug costs than with tricyclics but switching between antidepressants reduced this difference. The increase in the acquisition costs of fluoxetine may have been balanced by lower medical costs, although the study had limited power to estimate these costs precisely. This means that the study could not detect a difference in medical costs of about the same amount as the difference in drug costs. Therefore, although we can be fairly confident that first line fluoxetine led to a larger drug bill we are less certain about how overall costs compared between groups. Even if the costs balance, interpretation will depend on which budget you control and on your healthcare system.

The situation is complicated further because we cannot assume that results with fluoxetine will be the same with other SSRIs and new antidepressants. Were many of these patients with mainly mild depression appropriately given an antidepressant at all? The mean HDRS was at about the threshold below which antidepressants have not been shown to be beneficial1; half of these patients therefore could have had up to 2 years of unnecessary drug treatment. Targeting more severely ill patients is at least as important as choosing which antidepressant to use.

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